SS-220
a New Arthropod Repellent

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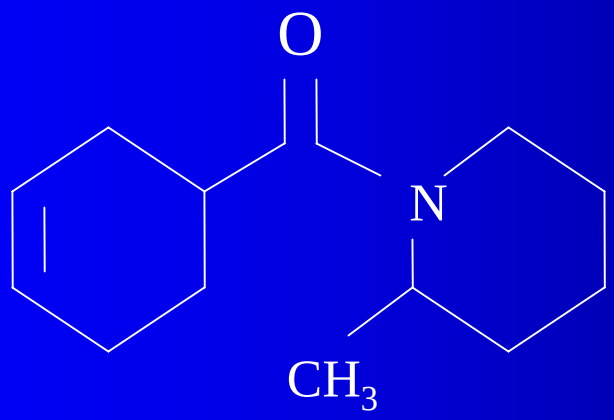
Introduction

- Arthropods (insects) and their impact on human health.
- Insect repellents and the war fighter.
- CHPPMs involvement in evaluation and development.

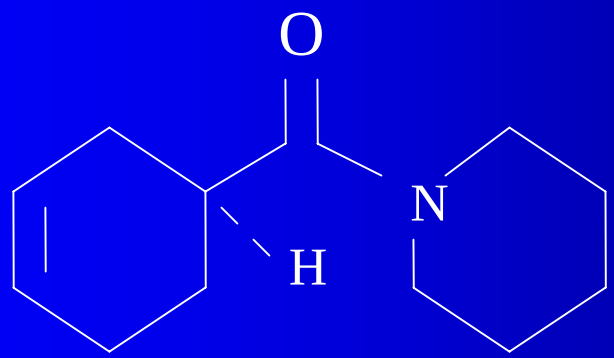
Structure of AI3-37220

1-(3-cyclohexen-1-ylcarbonyl)-2-methylpiperidine



Racemic AI3-37220

CAS No. 69462-43-7



SS-220

1S, 2S AI3-37220 isomer

Why Develop a New Standard Military Insect Repellent?

- ✓Current repellent has:
  - •Unpleasant application characteristics
  - •Low voluntary compliance
  - •Plasticizer
- ✓Availability of new active ingredients outperforming DEET
- ✓New technological advances in formulations

Historically……..

- 1812. Napoleon invasion of Russia
- War of 1812. Battle of New Orleans
- Civil War. 2:1 disease vs. combat
- WWII. Lost 24 mil man-days to bugs
- Vietnam. Lost 2 mil man-days malaria
- Somalia, Haiti, Americas, Middle East

Disease Vectors

Mosquitoes	*Aedes*	Yellow fever
		Dengue
		Viral encephalitis
	Anopheles	Malaria
Body lice	*Pediculus*	Epidemic typhus
Sand flies	*Phlebotomus*	Leishmaniasis
Ticks	*Dermacentor*	Spotted fevers
	Ixodes	Lyme disease
		Viral encephalitis

Disease Vectors

Chigger mites	*Leptothrombidium*	Scrub typhus
Fleas	*Xenopsylla*	Plague
		Murine typhus
Biting Midges	*Culicoides*	Vis Filariasis
Black flies	*Simulium*	Oncocerciasis
Bot flies	*Dermatobia*	Myiasis
Deer flies	*Chrysops*	Tularemia
Tsetses	*Glossina*	Myiasis

Annual Casualty Rates

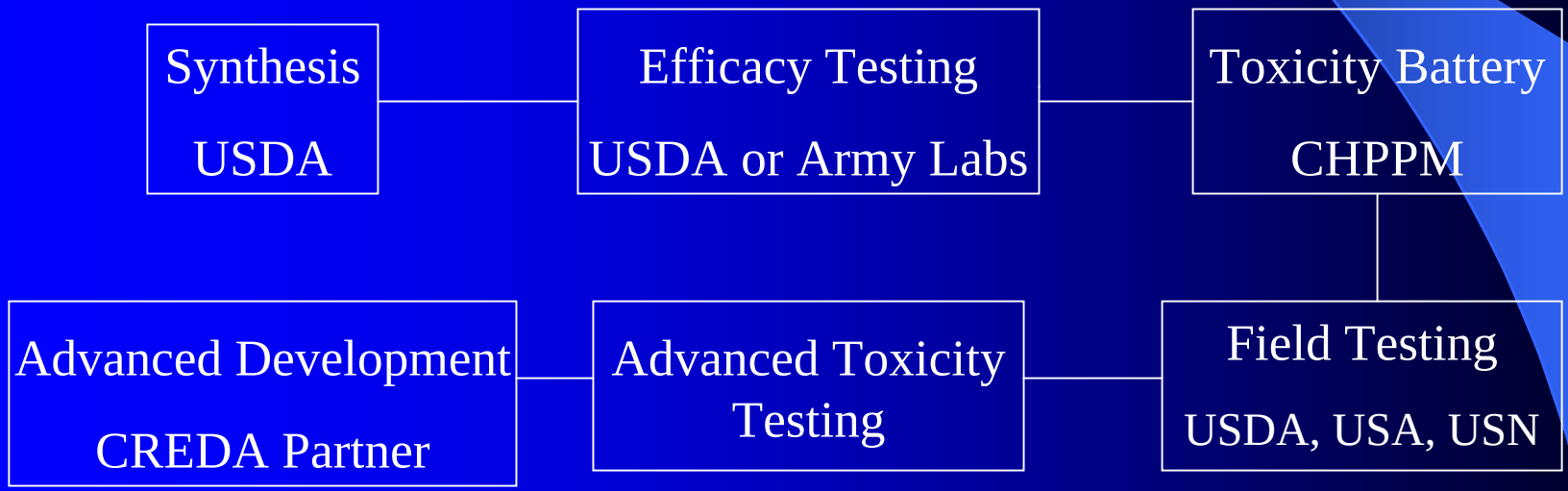
Disease	Cases	Deaths
Malaria	300-500 million	1-2 mil
Dengue	50 million	15,000
Yellow Fever	0.2 million	30,000
Leishmaniasis	1.5 – 2 million	

Milestones

- 1948. US Army develops Deet
- 1959-1995. Efficacy tests - 15,000 cmpnds
  Toxicity tests - 5,000 cmpnds
- 1978. USDA synthesizes AI3-37220
- 1986. Reformulate Deet into extended duration cream base (33% AI)
- 1994. Permethrin clothing treatment
- 2002. STO for SS-220 development

Repellents Development

MOU between US Army Medical Command, US Army OTSG, US Navy OTSG, Armed Forces Pest Management Board, and US Department of Agriculture



EPA 6-PAK

- ✓ 870.1100 acute oral
- ✓ 870.1200 acute dermal
- ✓ 870.2400 primary eye irritation
- ✓ 870.2500 primary skin irritation
- ✓ 870.2600 dermal sensitization
- ✓ 870.1300 acute inhalation

Tier I

- 870.3250 90-day dermal
- 870.3700 oral developmental (1st species)
- 870.6200 neurotoxicity screening battery
- ✓ 870.5265 Ames triple plate
- ✓ 870.5375 CHO chromosome aberration
- ✓ 870.5395 micronucleus assay
- ✓ 870. 5200 mouse lymphoma

Tier II

- 870.3100 90-day oral w/ neurotox
- 870.3700 oral developmental (2nd species)

Tier III

- 870.3800 oral reproduction/fertility-2 gen
- 870.4100 oral chronic toxicity-non rodent
- 870.4200 oral carcinogenicity (18 mo)
- 870.4300 combined oral chronic toxicity and carcinogenicity
- 870.7485 metabolism/pharmacokinetics
- 870.7600 dermal absorption - optional

Summary

- Historically, diseases caused by arthropods account for most wartime casualties. 2:1
- Insect repellents are the first line of defense.
- SS-220 appears to be best in over 50 years.
- Commercial potential
- Seek advanced development partners